FANCC gene

Fanconi anemia complementation group C

Normal Function

The *FANCC* gene provides instructions for making a protein that is involved in a cell process known as the Fanconi anemia (FA) pathway. The FA pathway is turned on (activated) when the process of making new copies of DNA, called DNA replication, is blocked due to DNA damage. The FA pathway is particularly responsive to a certain type of DNA damage known as interstrand cross-links (ICLs). ICLs occur when two DNA building blocks (nucleotides) on opposite strands of DNA are abnormally attached or linked together, which stops the process of DNA replication. ICLs can be caused by a buildup of toxic substances produced in the body or by treatment with certain cancer therapy drugs.

The FANCC protein is one of a group of proteins known as the FA core complex. The FA core complex is composed of eight FA proteins (including FANCC) and two proteins called Fanconi anemia-associated proteins (FAAPs). This complex activates two proteins, called FANCD2 and FANCI, by attaching a single molecule called ubiquitin to each of them (a process called monoubiquitination). The activation of these two proteins, which attach (bind) together to form the ID protein complex, attract DNA repair proteins to the area of DNA damage so the error can be corrected and DNA replication can continue.

Health Conditions Related to Genetic Changes

Fanconi anemia

At least 50 mutations in the *FANCC* gene have been found to cause Fanconi anemia, a disorder characterized by a decrease in bone marrow function, an increased cancer risk, and physical abnormalities. Mutations in the *FANCC* gene are responsible for about 15 percent of all cases of Fanconi anemia. A particular mutation in the *FANCC* gene has been found in people with Central and Eastern European (Ashkenazi) Jewish background. This mutation (written as 456+4A>T) disrupts the way the gene's instructions are used to make the protein. Individuals with this mutation tend to have more severe signs and symptoms than people who have some of the other mutations in the *FANCC* gene.

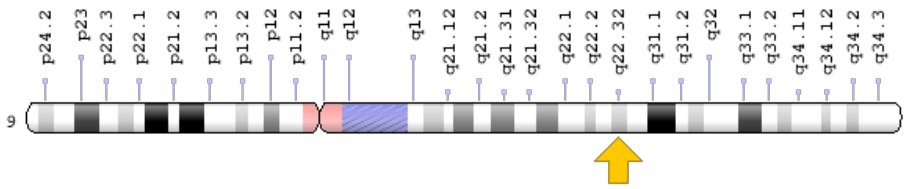
Most mutations in the *FANCC* gene that cause Fanconi anemia lead to absent or reduced protein function. As a result, the FA core complex cannot function and the entire FA pathway is disrupted. Due to the disrupted pathway, DNA damage is not repaired efficiently and ICLs build up over time. The ICLs stall DNA replication,

ultimately resulting in either abnormal cell death due to an inability make new DNA molecules or uncontrolled cell growth due to a lack of DNA repair processes. Cells that divide quickly, such as bone marrow cells and cells of the developing fetus, are particularly affected. The death of these cells results in the decrease in blood cells and the physical abnormalities characteristic of Fanconi anemia. When the buildup of errors in DNA leads to uncontrolled cell growth, affected individuals can develop leukemia or other cancers.

Chromosomal Location

Cytogenetic Location: 9q22.32, which is the long (q) arm of chromosome 9 at position 22.32

Molecular Location: base pairs 95,099,054 to 95,317,730 on chromosome 9 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- FAC
- FACC
- FANCC_HUMAN
- Fanconi anemia, complementation group C

Additional Information & Resources

Educational Resources

- Madame Curie Bioscience Database: FANCC
  https://www.ncbi.nlm.nih.gov/books/NBK6302/#A45462
- Madame Curie Bioscience Database: FANCC Gene Mutations
  https://www.ncbi.nlm.nih.gov/books/NBK6419/#A50955
- Madame Curie Bioscience Database: The FA "Nuclear Core Complex"
  https://www.ncbi.nlm.nih.gov/books/NBK6302/#A45480

GeneReviews

- Fanconi Anemia
  https://www.ncbi.nlm.nih.gov/books/NBK1401

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28FANCC%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- FANCC GENE
  http://omim.org/entry/613899

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/FACCID101.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=FANCC%5Bgene%5D
- HGNC Gene Family: Fanconi anemia complementation groups
  http://www.genenames.org/cgi-bin/genefamilies/set/548
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=3584
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/2176
- The Rockefeller University: Fanconi Anemia Mutation Database: FANCC
  http://www2.rockefeller.edu/fanconi/genes/jumpc
- UniProt
  http://www.uniprot.org/uniprot/Q00597

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